

PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (<http://bmjopen.bmj.com/site/about/resources/checklist.pdf>) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

TITLE (PROVISIONAL)	Prescriber barriers and enablers to minimising potentially inappropriate medications in adults: A systematic review and thematic synthesis
AUTHORS	Anderson, Kristen; Stowasser, Danielle; Freeman, Christopher; Scott, Ian

VERSION 1 - REVIEW

REVIEWER	Aoife Fleming School of Pharmacy University College Cork Ireland
REVIEW RETURNED	12-Sep-2014

GENERAL COMMENTS	<p>Point 13.</p> <p>It is noted that the authors appraised the included studies using the COREQ criteria.</p> <p>In terms of the reporting of this paper, if the authors have met the ENTREQ requirements for reporting the synthesis of qualitative research, it would be useful to see this.</p> <p>This paper is well written and deals with a very important issue which requires substantial qualitative investigation. The focus of the synthesis on reducing inappropriate prescribing is certainly useful for the development of future interventions in this area. There are several points which need to be addressed.</p> <p>1. A definition of PIM or PIP has not been provided. In the introduction the consequences of both are discussed but it is important to clearly set out what exact practice is being investigated in this review.</p> <p>2. The title states that this is a review in 'adults', however the introduction is largely focused on older adults. Table 1 indicates for some studies if they focus on elderly patients. It would be interesting to clarify in Table 1 whether the focus is the elderly or all ages etc. If non-elderly populations included then address this in the Introduction also.</p> <p>3. A detailed quality appraisal of included studies has been conducted, however, the reporting in Table 2 does not allow the reader to make an easy assessment of each individuals study quality. A more detailed review of each study assessment results would be useful in the Supplementary material. It is not reported whether the included studies had obtained ethics approval; please address.</p>
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	<p>4. Page 19, lines 5,6: it would be useful to report what the main findings of these studies were. There have been several recent studies investigating the discontinuation of antipsychotic medications in dementia patients for example. The impact of this qualitative paper would be enhanced if its relevance to other 'intervention' studies could be discussed.</p> <p>5. Page 12, line 38: in the quotation (42) who is being referred to as "they"?</p>
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REVIEWER	<p>Dr Emily Reeve University of Sydney, Australia</p> <p>I met the authors of this article earlier this year at the first Australian Deprescribing Network (ADeN) workshop where preliminary results of this work were presented. A publication is planned as an outcome of this workshop to be authored by Ian Scott and the ADeN (of which myself and the other authors of this article are members of, among with some 40+ members from around Australia). I have no conflict of interest regarding the publication of this article 'Prescriber barriers and enablers to minimising potentially inappropriate medications in adults: A systematic review and thematic synthesis'.</p>
REVIEW RETURNED	18-Sep-2014

GENERAL COMMENTS	<p>This is a comprehensive piece of work that is well planned and well written. The authors have completed a difficult task of synthesising the available work on this subject.</p> <p>Some minor comments that I feel will strengthen this piece of work.</p> <p>Page 2, line 41: Abstract conclusion – '... aimed at minimising potentially inappropriate prescribing ...' as the term prescribing may be interpreted as initiation of a medication as well as continued prescribing, suggest changing to '... aimed at increasing deprescribing of PIMs to reduce the risk of iatrogenic harm.' Or something similar as your review focuses on withdrawal not initiation of PIMs.</p> <p>Page 4: Introduction – you have introduced both the abbreviations PIP and PIM, as these terms have been used interchangeably in the past (though I concede can be argued to be two different things), for consistency throughout the article I think it would be best to use the term PIM and prescribing of PIMs in the place of PIP.</p> <p>Line 13, page 6: Methods – 'Two reviewers (DS, IS) independently read all papers and then iteratively assessed coded text and subthemes to ensure comprehensiveness and reliability of the findings [28].' Can you please clarify what you mean by this – did the two reviewers read over the codes which had been applied to the text by the first reviewer or did they independently apply the codes and group into themes?</p> <p>Line 39, page 6: Methods – 'and five for various PIMs' In table 1 you use the term 'Variety of different single medications', can you clarify what this means, were they a pre-specified list of medications? Perhaps calling this non-specific PIMs or PIMs in general may be more appropriate, but I will leave this up to you.</p> <p>Table 1: In the participants column several of the studies included non-prescribers, as you did not include the results from these</p>
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	<p>participants in this review perhaps it would be best to only include the participant details of those that were relevant to your review.</p> <p>Table 2 and 3: in your discussion you say 'Many subthemes were common to papers regardless of inter-study differences in the PIM/s discussed, patient age and clinical setting (e.g. primary, secondary or residential aged care).' Is it possible to add some of this detail to the tables, for example add an extra column with includes the medications/setting/age of interest that represented that sub-theme?</p> <p>Editing comments Line 10, page 2: Should abbreviation in abstract be 'PIMs' not 'PIM'? Line 24, page 5: Methods – '...focus entirely on initiation of PIM; s and 4) reported...' I believe the semicolon is in the wrong place</p>
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REVIEWER	Ravishankar Ramaswamy Icahn School of Medicine at Mount Sinai, New York, NY, USA
REVIEW RETURNED	22-Sep-2014

GENERAL COMMENTS	<p>Comprehensively done systematic review of a very important topic in geriatric medicine and pharmacotherapy. Overall, study selection, quality assessment of studies included and qualitative thematic analysis are clearly described and discussed.</p> <p>- Authors mention that those articles whose abstracts / full text that were not available were excluded. Was an attempt made to contact authors to obtain these articles if they were felt to be of interest and pertinence?</p> <p>Minor errors: - Page 11, 3rd column, 3rd row from the bottom, "heroin" spelled as "heroine". - Page 12, 3rd column, 2nd row from the top, 3rd comment should be italicized. "When house officers come to our ward,...."</p>
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VERSION 1 – AUTHOR RESPONSE

Review 1 -
Point 13.

It is noted that the authors appraised the included studies using the COREQ criteria.

In terms of the reporting of this paper, if the authors have met the ENTREQ requirements for reporting the synthesis of qualitative research, it would be useful to see this.

Actioned - Page 21, Line 50. Now listed as a strength of the study.

This paper is well written and deals with a very important issue which requires substantial qualitative investigation. The focus of the synthesis on reducing inappropriate prescribing is certainly useful for the development of future interventions in this area. There are several points which need to be addressed.

1. A definition of PIM or PIP has not been provided. In the introduction the consequences of both are discussed but it is important to clearly set out what exact practice is being investigated in this review.

Actioned - Page 4, lines 10&11.

2. The title states that this is a review in 'adults', however the introduction is largely focused on older

adults. Table 1 indicates for some studies if they focus on elderly patients. It would be interesting to clarify in Table 1 whether the focus is the elderly or all ages etc. If non-elderly populations included then address this in the Introduction also.

Actioned - Please see Table 1, column 7.

The introduction has also been amended - Please see Page 4, lines 15-19.

3. A detailed quality appraisal of included studies has been conducted, however, the reporting in Table 2 does not allow the reader to make an easy assessment of each individual's study quality. A more detailed review of each study assessment results would be useful in the Supplementary material.

Actioned - Supplementary Table detailing the Completion of the COREQ checklist has been provided. This is a working document adapted from an Excel Spreadsheet but has been uploaded as a Word document in line with BMJ Open's preference.

It is not reported whether the included studies had obtained ethics approval; please address.

Actioned - Page 10, line 17.

4. Page 19, lines 5,6: it would be useful to report what the main findings of these studies were.

Actioned - Page 21, Line 36-37

There have been several recent studies investigating the discontinuation of antipsychotic medications in dementia patients for example. The impact of this qualitative paper would be enhanced if its relevance to other 'intervention' studies could be discussed.

Response - The range of deprescribing intervention studies to date is diverse (spans intervention studies from improving prescribing generally to stopping or reducing single PIMs and to a lesser extent, reducing potentially inappropriate polypharmacy in the non-palliative care setting). It would be difficult to justify making reference to specific papers (e.g. discontinuation of antipsychotic medications) and not others. Discussing the broad range of intervention studies would require a paper in itself, one we are keen to consider. Page 22, lines 6-8 we have simply identified that the exploration of barriers and enablers has been lacking in studies to date.

Reviewer: 2

Reviewer Name Dr Emily Reeve

Institution and Country University of Sydney, Australia

Please state any competing interests or state 'None declared': I met the authors of this article earlier this year at the first Australian Deprescribing Network (ADeN) workshop where preliminary results of this work were presented. A publication is planned as an outcome of this workshop to be authored by Ian Scott and the ADeN (of which myself and the other authors of this article are members of, among with some 40+ members from around Australia). I have no conflict of interest regarding the publication of this article 'Prescriber barriers and enablers to minimising potentially inappropriate medications in adults: A systematic review and thematic synthesis'.

This is a comprehensive piece of work that is well planned and well written. The authors have completed a difficult task of synthesising the available work on this subject.

Some minor comments that I feel will strengthen this piece of work.

Page 2, line 41: Abstract conclusion – '... aimed at minimising potentially inappropriate prescribing ...' as the term prescribing may be interpreted as initiation of a medication as well as continued prescribing, suggest changing to '... aimed at increasing deprescribing of PIMs to reduce the risk of iatrogenic harm.' Or something similar as your review focuses on withdrawal not initiation of PIMs.

Actioned - Page 2, lines 40-41.

Page 4: Introduction – you have introduced both the abbreviations PIP and PIM, as these terms have been used interchangeably in the past (though I concede can be argued to be two different things), for consistency throughout the article I think it would be best to use the term PIM and prescribing of PIMs in the place of PIP.

Actioned - the term PIMs has now been used consistently throughout the article in place of PIP.

Line 13, page 6: Methods – ‘Two reviewers (DS, IS) independently read all papers and then iteratively assessed coded text and subthemes to ensure comprehensiveness and reliability of the findings [28].’ Can you please clarify what you mean by this – did the two reviewers read over the codes which had been applied to the text by the first reviewer or did they independently apply the codes and group into themes?

Revised – Page 6, lines 18-19.

Line 39, page 6: Methods – ‘and five for various PIMs’ In table 1 you use the term ‘Variety of different single medications’, can you clarify what this means, were they a pre-specified list of medications? Perhaps calling this non-specific PIMs or PIMs in general may be more appropriate, but I will leave this up to you.

Actioned - Clarification of meaning has been provided on Page 6, lines 43-44. We have now adopted the terminology ‘miscellaneous PIMs’ in Table 1 and throughout the document.

Table 1: In the participants column several of the studies included non-prescribers, as you did not include the results from these participants in this review perhaps it would be best to only include the participant details of those that were relevant to your review

Actioned - This information has now been removed.

Table 2 and 3: in your discussion you say ‘Many subthemes were common to papers regardless of inter-study differences in the PIM/s discussed, patient age and clinical setting (e.g. primary, secondary or residential aged care).’ Is it possible to add some of this detail to the tables, for example add an extra column which includes the medications/setting/age of interest that represented that sub-theme?

Actioned - Please see column 3 which has been newly incorporated into Tables 3 & 4 (rather than 2 & 3 which we suspected was a typo) as requested.

Editing comments

Line 10, page 2: Should abbreviation in abstract be ‘PIMs’ not ‘PIM’?

Actioned - Abbreviation now amended to PIMs.

Line 24, page 5: Methods – ‘...focus entirely on initiation of PIM; s and 4) reported...’ I believe the semicolon is in the wrong place

Actioned.

Reviewer: 3

Reviewer Name Ravishankar Ramaswamy

Institution and Country Icahn School of Medicine at Mount Sinai, New York, NY, USA

Please state any competing interests or state ‘None declared’: None declared

Comprehensively done systematic review of a very important topic in geriatric medicine and pharmacotherapy. Overall, study selection, quality assessment of studies included and qualitative thematic analysis are clearly described and discussed.

- Authors mention that those articles whose abstracts / full text that were not available were excluded. Was an attempt made to contact authors to obtain these articles if they were felt to be of interest and pertinence?

Response: Due to the poor indexing of search terms for this topic, the principle author had a very low threshold for screening the abstract and full text of articles whose title offered even a glimmer of relevance to the review. In instances where no abstract was available, the full text was sought and largely revealed opinion pieces or conference abstracts/proceedings which were not eligible for inclusion. Efforts were not made to contact authors in instances where the full text was not available but re-review of search record titles (all of which are stored in an Endnote library) did not suggest any missed opportunities as a result of this.

Minor errors:

- Page 11, 3rd column, 3rd row from the bottom, "heroin" spelled as "heroine".

Actioned - This was the spelling provided in the original paper but has been changed as we accept it is a typographical error.

- Page 12, 3rd column, 2nd row from the top, 3rd comment should be italicized. "When house officers come to our ward,...."

Actioned.

VERSION 2 – REVIEW

REVIEWER	Aoife Fleming University College Cork, Ireland.
REVIEW RETURNED	04-Nov-2014

GENERAL COMMENTS	The authors have satisfactorily addressed the issues raised in the first review.
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REVIEWER	Dr Emily Reeve University of Sydney, Australia As per my first review of this manuscript I declare the following: I met the authors of this article earlier this year at the first Australian Deprescribing Network (ADeN) workshop where preliminary results of this work were presented. A publication is planned as an outcome of this workshop to be authored by one of the authors of this paper (IS), myself and other members of the ADeN.
REVIEW RETURNED	27-Oct-2014

GENERAL COMMENTS	I have no further comments on this manuscript.
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REVIEWER	Ravishankar Ramaswamy, MD Icahn School of Medicine at Mount Sinai, New York, USA
REVIEW RETURNED	30-Oct-2014

GENERAL COMMENTS	Appreciate author's response to reviewer comments and editing of manuscript.
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